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June 23, 2004

Michael O. Leavitt, Administrator
U.S. Environmental Protection Agency
Ariel Rios Building, 1101-A
1200 Pennsylvania Ave., N.W.
Washington, DC 20460

Subject: Comments on the HPV Test Plan for 1-(4-chlorophenyl)-4,4-dimethyl-3-pentanone

Dear Administrator Leavitt:

The following comments on Bayer's test plan for the chemical 1-(4-chlorophenyl)-4,4-dimethyl-3-pentanone are submitted on behalf of the Physicians Committee for Responsible Medicine (PCRM), People for the Ethical Treatment of Animals (PETA), the Humane Society of the United States (HSUS), the Doris Day Animal League, and Earth Island Institute. These health, animal protection, and environmental organizations have a combined membership of more than ten million Americans.

Bayer CropScience LP submitted its test plan on December 29, 2003 for the chemical 1-(4-chlorophenyl)-4,4-dimethyl-3-pentanone (CAS No. 66346-01-8), also referred to as HWG alkylketone. This compound is used as an intermediate in the production of an agricultural fungicide. Bayer has classified this chemical as a closed system intermediate, eliminating the requirement of a repeated dose and reproduction study under the HPV program. The sponsor has asked that a description of closed system intermediate status for this substance remain confidential and we are hopeful that Bayer has provided the EPA with all the relevant information to support this claim.

At this time, we question Bayer's proposal to conduct a developmental toxicity test, OECD 414, on HWG alkylketone that will result in the death of at least 1,300 animals. At the very least, if Bayer insists on conducting tests for developmental toxicity on this specific compound, we strongly urge the use of OECD 421, the combined reproduction/developmental screen, which will reduce animal deaths by half. The combined protocol is adequate for a screening level program such as HPV and is recommended by the EPA in the Federal Register Notice (FR/Vol. 65, No. 248, Tuesday December 28, 2000).

We are concerned that Bayer has made absolutely no attempt to bridge the data gap for developmental toxicity with existing data from similar or analogous chemicals. Specifically, Bayer does not specify any structurally similar compounds to HWG alkylketone in its test plan. Furthermore, Bayer does not provide any information as to

how this chemical might be related to a fungicide with similar structure, e.g. HWG 1608, also known as Tebuconazole(+-) (CAS No. 107534-96-3). We recognize that tebuconazole contains a 1,2,4-triazole side chain but data on the developmental effects and potential carcinogenicity of tebuconazole are available. Additional animal testing with HWG alkylketone could be avoided by drawing on the tebuconazole database. We ask that Bayer review all the available data for tebuconazole as this information might be used to bridge the data gap for developmental toxicity of HWG alkylketone. For instance, PCRM has identified two teratogenicity studies on tebuconazole; one of which was conducted by Bayer itself and both studies have been submitted to the EPA[1,2]. Details of these studies were not available to PCRM at the time these comments were prepared.

We are dismayed that the sponsor failed to identify these studies and we strongly urge Bayer to review the toxicity data for tebuconazole in order to avoid separate and/or duplicative testing for the developmental toxicity endpoint for HWG alkylketone. Without this analysis, it is otherwise completely unwarranted and premature to conduct further animal tests, which would kill many animals and only serve as a "check-the-box" exercise. Thank you for your attention to these comments. I may be reached at 202-686-2210, ext. 327, or via e-mail at *meven@pcrm.org*.

Sincerely,

Megha Even, M.S.
Research Analyst

Chad B. Sandusky, Ph.D.
Director of Research

References

1. Bayer AG. Embryotoxicity study with HWG 1608 technical in the rabbit including teratogenicity with cover letter dated 061588. EPA/OTS Document #88-880000046. 1988.

2. Research & Consulting Co. Oral teratogenicity range-finding study with rabbits on HWG 1608 technical (CAS No. 107534-96-3) (Final Report) with attachments and cover letter dated 080488. EPA/OTS Document #89-880000225. 1988